REMARKS

I. **Status of Claims**

Prior to the present amendment, Claims 28, 35-37, 40, and 41 are pending in the application and are rejected in the present Office Action. New Claim 43 is added by the present amendment.

Claims 28-42 were under examination in the previous Office action mailed June 6, 2005. The previous Office Action rejected claims 28, 30 and 35-42 rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Jao et al. (US 5,660,861), rejected claims 28, 30, 35-37, 40 and 41 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Jao et al. and Giacin et al. (US 5,302,373, and rejected claims 28 and 35-42 as being unpatentable over Jao et al. and Robson et al. (US 4,126,684). Applicant filed a reply on November 7, 2005, which cancelled claims 29-34. The Examiner indicated in the present Office Action that in light of the Applicant's reply, the § 102(b) rejection to claims 28, 36, 40 and 41 over Jao et al. and the § 103(a) rejection to claims 28 and 35-42 over Jao et al. and Robson et al. have been withdrawn. The sole rejection/objection that has been raised in the present Office action is rejection to Claims 28, 35-37, 40, and 41 under 35 U.S.C. §103(a) over Jao et al. (US Patent 5,660,861) and Giacin et al. (US 5,302,373).

II. **Amendments to the Claims**

Claims 28, 35, 37, and 41 have been amended to replace the term "humectant" with "propylene glycol." As in these claims the recited "humectant" refers to "propylene glycol," the amendment does not add new matter. Claim 43 is added, which depends from claim 28 and includes a further limitation regarding the relative content of the lactam formed under certain storage conditions. Support to new claim 43 can be found in the application as originally filed, such as Examples 1 through 10. Therefore, no new matter is added by claim 43.

## III. Claim Rejections under 35 U.S.C. §103

The Examiner alleges that claims 28, 35-37, 40, and 41 are unpatentable under 35 U.S.C. §103(a) over Jao et al. (US Patent 5,660,861) and Giacin et al. (US 5,302,373). Applicant respectfully submits that the rejection is improper for the following reasons.

### A. Non-analogous Prior Art

Applicant respectfully submit that US 5,302,373 (Giacin et al.) is not an analogous prior art and, therefore, can not be relied on as a basis for rejection of the application. An art is not analogous if it is neither in the field of the Applicant's endeavor, nor reasonably pertinent to the particular problem with which Applicant was concerned. MPEP 2141.01. The claimed invention relates to drug products for treating a disease. In the United States drug products are highly regulated under the federal law and subject to FDA review and approval for safety and efficacy prior to marketing. In contrast, US 5,302,373 relates to a cosmetic product. Specifically, it relates to non-drug, liquid cosmetic mouthwash for cleansing and refreshing the oral cavity. (See, for example, Abstract and column 1, line 6-14). In the United States cosmetic products do not require FDA review and approval for safety or efficacy prior to marketing. Therefore, US 5,302,373 is not in the same field of the Applicant's endeavor.

Moreover, US 5,302,373 is not reasonably pertinent to the particular problem with which Applicant was concerned. As disclosed in the specification, one particular problem with which Applicant was concerned is the degradation of 4-amino-3-substituted butanoic acid derivative (the active therapeutic agent) into toxic corresponding lactam in a solid finished product and the development of a stabilized solid composition for the active therapeutic agent (see, for example, "Background of the Invention"). Applicants have made earnest studies to solve the problem and found that the degradation of the 4-amino-3-substituted butanoic acid derivative can be prevented by addition of a stabilizer, such as propylene glycol. (see "Summary of the Invention") In contrast, US 5,302,373 was concerned with effective inclusion, in a liquid mouthwash, of an alkali metal bicarbonate that "provides deodorizing and buffering activities" and "contributes a clean mouthfeel and refreshing aftertaste in the oral cavity." (See, for example, column 1, lines

6-57). US 5,302,373 specifically teaches the inclusion of propylene glycol as a humectant to "add[s] body and a pleasant mouthfeel to the liquid mouthwash medium." (column 2, lines 29-33). Therefore, US 5,302,373 and Applicant are dealing with totally different problems. Because US 5,302,373 is neither in the field of the Applicant's endeavor, nor reasonably pertinent to the particular problem with which Applicant was concerned, it is not an analogous art.

**B. Non-establishment of *prima facie* Case of Obviousness**

Even if, *arguendo*, US 5,302,373 (Giacin et al.) could be properly relied upon, Applicant believes that, for reasons of record and further reasons detailed below, Examiner still has not established a *prima facie* case of obviousness. (MPEP §2143).

First, Applicant respectfully submits that there is no adequate motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine the reference teachings. Jao et al. relate to a dosage form that comprises an antiepileptic drug, sorbitol as an "osmagent," and exterior coating. The Examiner admitted that the composition of Jao et al. do not include a humectant that is propylene glycol. Giacin et al. disclose a mouth wash composition, which comprises a humectant such as propylene glycol and sorbitol. As the Examiner admitted, Giacin et al. further teach that the humectant is included to "add[s] body and a pleasant mouth feel to the liquid mouthwash medium." (See column 2, lines 28 and 29) The Examiner has alleged that "one skilled in the art would have been motivated to include a type of humectant that is propylene glycol in the composition of Jao et al. "for the advantage of providing a humectant that adds body and a pleasant mouth feel (Giacin: col. 2, lines 29-33) since both Jao et al. and Giacin et al. disclose pharmaceutical excipient such as sorbitol." (emphasis added). Applicant submits, however, that the Examiner has not presented a convincing line of reasoning why adding "body and a pleasant mouth feel" and the disclosure of sorbitol as a pharmaceutical excipient would adequately motivate a skilled artisan to include different excipient, i.e., propylene glycol, to a solid composition that is intended to be swallowed. As noted above, the claimed

invention is a solid composition while Giacin et. al. relate to a liquid mouthwash. While Giacin et. al. teach that a humectant "adds body and a pleasant mouth feel" to a liquid mouthwash, neither reference has any teaching, nor has the Examiner alleged that it is within the knowledge of a person skilled in the art, that propylene glycol would add "body and a pleasant mouth feel" to a solid composition. Absent such teaching or knowledge, a person skilled in the art would have no reason to include propylene glycol to a solid composition in order to add body and a pleasant mouth feel to it.

Further, neither reference suggests any desirability of adding "body and a pleasant mouth feel" to a solid composition of Jao et. al. Giacin et al. teach a liquid mouthwash for use for "rinsing the oral cavity" and to "cleanse and refresh the oral cavity." (Abstract and column 1, lines 6-8). Therefore, the liquid mouthwash is intended for full contact with the oral cavity. Accordingly, it is understandable that "body and a pleasant mouth feel" would be desirable for the mouthwash. However, the composition of Jao et. al., as noted in the Office action, is a solid dosage form of tablet or capsule. Such a tablet or capsule is intended to have only minimal contact with the oral cavity. The references do not suggest any meaningful advantage of adding body and mouth feel to such as solid.

Similarly, Applicant submits that the mere fact that both Jao et al. and Giacin et al. disclose sorbitol as a pharmaceutical excipient does not provide adequate motivation to a skilled artisan to use a different agent, i.e. propylene glycol, in the claimed invention. Specifically, according to Giacin et al., the purpose of including sorbitol or propylene glycol in the mouthwash is for adding "body and a pleasant mouth feel." In contrast, the purpose of including sorbitol in the solid dosage form of Jao et al. is "for contributing the delivery kinetics of the antiepileptic drug." (Jao et al., column 7, lines 41-52). Neither reference teach nor suggest that propylene glycol would serve the same purpose of "contributing the delivery kinetics of the antiepileptic drug" as sorbitol. Absent such teaching or suggestion, a person skilled in the art would not be motivated to substitute propylene glycol for sorbitol in the solid composition of Jao et al. to arrive at the claimed invention.

Moreover, Applicant respectfully submits that the proposed combination of the references do not have a reasonable expectation of success. The Examiner has alleged that one of ordinary skill in the art would have reasonable expectation of success in the combination of Jao et al. and Giacin et al. "because Giacin et al. disclose that sorbitol, propylene glycol, and glycerol are functionally equivalent humectant (Giacin: col. 2, lines 29-33)." (emphasis added). As noted above, the purpose of using sorbitol or propylene glycol in the liquid mouthwash of Giacin et al. is different from the purpose of using sorbitol in the solid osmotic dosage form of Jao et al. It is settled that listing several compounds as equivalents for one purpose will not establish their equivalency for all purposes. (see *In re Jezl*, 396 F.2d 1009, 158 USPQ 98 (CCPA 1968)). Therefore, even if sorbitol, propylene glycol, and glycerol have equivalent function of adding "body and a pleasant mouthfeel" to a liquid mouthwash, it does establish that sorbitol and propylene glycol have an art-recognized equivalent function of "contributing to the delivery kinetics of the antiepileptic drug" in the osmotic solid dosage form." Therefore, a person skilled in the art would not have a reasonable expectation of success to replace sorbitol with propylene glycol in the solid composition of Jao et al. to arrive at the claimed invention.

Finally, Applicant respectfully submits that, even assuming that the cited references could be combined, they do not teach or suggest all the claim limitations. For example, claim 41 recites a process for stabilizing a solid composition containing the 4-amino-3-substituted butanoic acid derivative. Neither reference suggests that propylene glycol would stabilize the solid composition of Jao et al. Further, new claim 43, which depends from claim 28, includes a further element "wherein after storage of the composition in a sealed container at 60°C for 2 weeks the content of the corresponding lactam that is formed in the composition is less than 0.20% by weight relative to the initial amount of the 4-amino-3-substituted-butanoic acid derivative in the composition." The references, individually or in combination, do not teach or suggest this element either.

**C. Non-obviousness of the Claimed Invention as a Whole**

The Examiner has stated in the present Office Action that Applicant's arguments submitted in the previous reply filed on 07 November 2005 traversing the rejection under 35 U.S.C. 103(a) as being unpatentable over Jao et al. and Giacin et al. were are not persuasive. The Examiner gave two reasons. Applicant respectfully offers the following comments regarding the reasons given by the Examiner.

In the reply filed on 07 November 2005, Applicant argued that the claimed invention has unexpected results and, therefore, would not have been obvious over the cited references. To support the argument, Applicant pointed, as evidence, to the examples in the specification presenting comparative data as demonstrating that adding propylene glycol to solid compositions containing gabapentin or pregabalin prevents lactam formation, and thus stabilizes the solid composition. In the present Office Action the Examiner responded that objective evidence of unexpected results "must be factually supported by appropriate affidavit or declaration to be of probative value," citing *In re DeBlauwe*, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir.1984). Apparently, the Examiner did not consider the comparative data in the specification because they are not supported by a declaration or affidavit. Here, Applicant respectfully submits that in determining obviousness the Examiner is required to consider the claimed invention as a whole, which in turn requires looking not only to the subject matter which is literally recited in the claim in question "but also to those properties of the subject matter which are inherent in the subject matter and are disclosed in the specification." *In re Antonie*, 559 F.2d 618, 619, 195 U.S.P.Q. 6, 8 (C.C.P.A. 1977). The enhanced stability of the claimed solid composition is a property inherent in the claimed invention and is disclosed in the specification. Therefore, this property should be considered in determining whether or not the claimed invention is obviousness. Moreover, Applicant respectfully submits that the Examiner is required to consider the comparative data in the specification in determining the patentability under 35 U.S.C. 103(a), even if they are not supported by a declaration or affidavit. In this regards, Applicant respectfully draws the Examiner's

attention to *In re Margolis*, 785 F.2d 1029, 228 USPQ 940 (Fed. Cir. 1986) and MPEP 716.01(a).

Applicant notes the Examiner comments, "Lastly, any differences between the claimed inventions and the prior art may be expected to result in some differences in properties. The issue is whether the properties differ to such an extent that the difference is really unexpected." Applicant respectfully submits that the comparative data in the examples, together with other disclosure, in the specification clearly show that the enhanced stability of the claimed invention is truly unexpected. Specifically, the specification on pages 3 through 5 discloses that pharmaceutical preparations containing gabapentin or similar 4-amino-3-substituted-butanoic acid derivatives are difficult to prepare because the active ingredient readily undergoes degradation to form corresponding lactam. The specification on page 5 further discloses that, due to toxicity of the lactam, it is desirable to keep the lactam content to a minimal level. The comparative data disclosed in the examples show that addition of propylene glycol to the composition reduced the formation of the corresponding lactam, thus stabilizing the composition. The specification at the last paragraph (before the Claims) discloses:

> It has been believed that an excess water remaining generally in solid preparations including a preparation of the 4-amino-3-substituted butanoic acid derivative would be undesirable since it may cause discoloration, degradation, tableting troubles or the like. It is the most significant feature of this invention that, unexpectedly, a stability of a solid preparation of the 4-amino-3-substituted-butanoic acid derivative can be remarkably improved by the addition of a humectant which has a water retention activity and has been considered to trigger unfavorable disturbances in the said preparation as stated above. (emphasis added)

Thus, the specification has clearly disclosed that the enhanced stability is a superior property of the claimed invention and is totally unexpected. Accordingly, the claimed invention would not have been obvious to a person skilled in the art.

In arguing that the cited references do not suggest the modification or provide a reasonable expectation of success, but "at most, the references represent an obvious to try rationale, which cannot render the claims obvious" under 35 U.S.C. §103(a), Applicant

submitted, "None of the references even hint that humectants such as propylene glycol will stabilize formulations containing gabapentin or pregabalin. The references list a few humectants among many excipients. These excipients belong to many different classes and serve many different purposes in pharmaceutical formulations. . . . The references provide little guidance as to which excipients will or will not stabilize gabapentin or pregabalin." The Examiner responded in the present Office Action, "Second in response to applicant's argument that 'the references list a few humectants among many excipients', the examiner recognized that a genus does not always anticipate a claim to a species within the genus. However, when the species is clearly named, the species claim is anticipated no matter how many other species are additionally named. . . . In this case, Giacin et al. clearly cited the species of propylene glycol." (Office action, page 7) Applicant totally agrees with the Examiner that Giacin et al. would anticipate a claim to propylene glycol. However, Applicant respectfully submits that anticipating a claim to propylene glycol does not provide the requisite suggestion and reasonable expectation of success to combine the references' teaching to arrive at the claimed invention. Absent such suggestion and reasonable expectation of success, the references can not render the claimed invention obvious.

## IV. Concluding Remarks

In view of the amendments and the foregoing remarks, Applicant respectfully requests reconsideration of the matter and the withdrawal of all the rejections/objections. Applicant believes that the application is now in order for allowance and, accordingly, respectfully requests timely issuance of a Notice of Allowance.

Respectfully submitted,

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